

AMENDMENTS TO THE DRAWINGS

The attached sheet of drawings includes changes to Figure 1. The label “Figure 1” has been deleted at the Office’s request pursuant to 37 C.F.R. § 1.84(u)(1). No other changes to the drawings have been made.

Attachment: Replacement sheet

REMARKS**Status of the Claims**

Claims 1-24 are currently pending in this application. In this amendment, claims 13 and 22 have been canceled without prejudice or disclaimer; claims 1, 2, 4, 6, 8-12 and 15-21 have been amended to clarify the invention; and new claims 23 and 24 have been added. Support for the amendment may be found in the application as filed (WO 2005/017193) at least at page 2, lines 15-16; page 7, lines 3-6; page 8, lines 1-3; page 19, lines 4-12; page 22, lines 1-5 and 13-14; page 24, lines 9-10; and in the original claims 13 and 22, now canceled. No new matter has been added. Upon entry of the amendment, claims 1-12, 14-21, 23 and 24 will be pending. Entry of the amendment and reconsideration on the merits are respectfully requested.

Objection to the Drawings

Corrected drawings in compliance with 37 C.F.R. § 1.121(d) are required because of the application's alleged failure to comply with 37 C.F.R. § 1.84(u)(1), which states: "Where only a single view is used in an application to illustrate the claimed invention, it must not be numbered and the abbreviation "FIG." must not appear."

In this response, the label "Figure 1" has been removed from the drawings pursuant to 37 CFR 1.84(u)(1). No other changes to the drawings have been made. A Replacement Sheet is provided herein according to 37 C.F.R. § 1.121(d). Applicants respectfully request that this objection be withdrawn.

Objection to the Specification

The specification is objected to because of the following informalities:

- a. At page 22, line 25, there appears to be an instance of an unrecognized character being part of the abbreviation for a unit of measure;

and

b. At page 23 there are representations of nucleotide sequences that are not accompanied with the requisite SEQ ID NO.

With regard to the first objection, the specification has been amended herein to correct the inadvertent typographical error that occurred during the transmission of the parent PCT application.

With regard to the second objection, the Office is respectfully referred to a Preliminary Amendment filed March 10, 2008 wherein SEQ ID NOS were added to each of the nucleotide sequences listed in Table 1.

Accordingly, both objections have been overcome and may properly be withdrawn.

Rejection under 35 U.S.C. § 112, First Paragraph

Claims 1-22 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. The claims are alleged to contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

“The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.” *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). MPEP 2164.01. A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984). “As long as the specification discloses at least one method for making and using the claimed invention that bears a

reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112, is satisfied.” *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (CCPA 1970). MPEP § 2164.01(b) (emphasis added).

In this case, the Office appears to have taken an unacceptably aggressive view of claim construction, interpreting claims to encompass things that were clearly never intended to be covered. For example, in paragraph 8 of the OA, the Office states: “Recognizing that claim, 1 must encompass more than those embodiments set forth in claim 13, claim 1 is construed as also encompassing viral nucleic acids (DNA and RNA).” However, there is not a single mention of viral nucleic acids in the entire application; and both the specification and claim 1 expressly refer to cell lysis. Moreover, the specification at page 7, lines 16-18 states: “In some embodiments, the biological sample is a non-virus biological organism, a biological tissue, a eukaryotic cell, or a prokaryotic cell.” Nevertheless, to clarify the invention, claim 1 has been amended herein to specify that the target nucleic acid is bacterial rRNA.

In paragraph 10 of the OA, the Office further states: “The method of claims 1-22 has also been construed as encompassing the detection of mutations (point mutations (insertions and/or deletions), translocations, and inversions).” Additionally, it is stated in paragraph 21 of the OA: “The claimed method has been construed as encompassing sequencing a nucleic acid via hybridization.” This claim construction is patently absurd. There is no mention of sequencing or detection of mutations in the entire application. On the contrary, the application clearly states: “The method of the invention can be generally used in nucleic acid detections, for example, detection and identification of clinical bacteria, detection of drug-resistant bacteria, environmental detection, forensic detection, and analysis of gene expression, etc. Moreover, claim 1 specifies that the goal of the claimed method is “to determine the presence, absence and/or amount” of the target nucleic acid molecule. It is not clear to Applicants how the Office has managed to accomplish the logical leap from “determining the presence, absence and/or amount” of a target nucleic acid molecule to “detecting point mutations” and “gene sequencing.” This construction certainly goes far beyond the “broadest reasonable interpretation”.

Applicants are concerned that the Office seems to have missed the entire point of the present invention. This application is not about a novel microarray technology platform. It is primarily about new methods of improving the speed and efficiency of bacterial detection by eliminating the nucleic acid purification step prior to hybridization on a diagnostic microarray. The key objectives and technical advantages of the present invention are stated clearly in the application:

The rapid detection of nucleic acids molecule is important for research in life science and clinical diagnosis, especially in clinical diagnosis of infectious diseases. For example, the detection of infectious bacteria in hospital needs culture, pure culture and several biochemical detections, which takes several days and is disadvantageous for patient. The present invention provides a rapid method which takes no more than 90 minutes to get a clear and accurate result. The present invention only takes two steps (the lysis of biological samples and hybridization with microarrays to get clearly results, and can be easily applied in miniaturization and automation systems.

(WO 2005/017193 at page 2, lines 11-18, emphasis added).

The object of the present invention is to provide a rapid method to detect nucleic acids by the direct hybridization of cellular lysate with microarrays without any further purification. This method is simple, low-cost, convenient-to-operate, contamination-free, and easy-to-integrate.

(WO 2005/017193 at page 2, lines 21-24, emphasis added).

The bacterial detection needs more than 5-7 days using conventional methods in hospital. However, in the present example, it only took 1.5 hr to get accurate results by hybridizing directly the cell lysate with probes on microarrays. In addition, the detection sensitivity of the present example, is as high as 10^5 cfu/mL, which is helpful to the rapid diagnosis and proper treatment of patients.

(WO 2005/017193 at page 24, lines 8-12, emphasis added).

The working example on pages 22-24 demonstrates the claimed invention in action. It clearly illustrates quantitative detection of different titers of *Staphylococcus aureus* cells by specific hybridization of target *S. aureus* rRNA with a capture DNA probe tethered to microarray surface

and with a Hex-modified reporter DNA probe (*see* pages 22-24 and the accompanying drawing). The working example clearly bears a reasonable correlation to the entire scope of the claims 1-12, 14-21, 23 and 24 as amended, which is all that is required under the rule of *In re Fisher* to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph. A person skilled in the art would have had no difficulty practicing the claimed invention given the guidance provided in the application and the high level of skill in the field of microarrays at the time of the invention. *See, e.g.*, the section “Immobilization of probes” at pages 12-16 of the instant application and the publications cited therein; *see also* A. Marshall & J. Hodgson, “DNA chips: An array of possibilities,” *Nat. Biotechnol.*, 16:27-31 (1998), attached herein as **Exhibit A**; G. Ramsay, “DNA chips: State-of-the-art,” *Nat. Biotechnol.*, 16:40-44 (1998), attached herein as **Exhibit B**; R.W. Ye *et al.*, “Applications of DNA microarrays in microbial systems,” *J. Microbiol. Meth.*, 47:257-272 (2001), attached herein as **Exhibit C**; M.J. Heller, “DNA Microarray Technology: Devices, Systems, and Applications,” *Annu. Rev. Biomed. Eng.*, 4:129–53 (2002), attached herein as **Exhibit D**.

In view of the foregoing, the instant claims as amended are adequately enabled by the disclosure in the specification in combination with the common knowledge in the art at the time of the invention. Accordingly, Applicants respectfully submit that this rejection under 35 U.S.C. § 112, first paragraph may properly be withdrawn.

Rejection under 35 U.S.C. § 112, Second Paragraph

Claim 19 is rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claim 19 is rejected for its recitation of “a four-dimensional array.”

Claim 19 has been amended to delete the phrase “a four-dimensional array,” thereby rendering this rejection moot. Accordingly, this rejection under 35 U.S.C. § 112, second paragraph may also properly be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. **514572001600**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

Electronic signature: /Yan Leychkis/
Yan Leychkis

Registration No.: 60,440
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100
San Diego, California 92130-2040
(858) 314-7702